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EXAMINER

KATCHEVES, KONSTANTINA T

ART UNIT PAPER NUMBER

1636

DATE MAILED: 10/06/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/809,456

Applicant(s)

MADRY ET AL.

Examiner

Konstantina Katcheves

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 21 July 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1, 2 and 4-52 is/are pending in the application.
- 4a) Of the above claim(s) 22-42, 46 and 51 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 4-21, 43-45, 47-50, 52 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 46, 51 are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 13. 6) ☐ Other:

### **DETAILED ACTION**

Claims 1, 2 and 4-52 are pending in the present application. Claims 22-42 and new claims 46 and 51 are withdrawn from consideration. Accordingly claims 1, 2 and 4-21 and new claims 43-45, 47-50 and 52 are currently under examination. This Office action is in response to Applicant's amendment and response filed 21 July 2003.

#### ***Election/Restrictions***

Newly submitted claims 46 and 51 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The present claims are drawn to *ex vivo* gene therapy method which are biologically and functionally different and distinct from each other and thus one does not render the other obvious. Because newly filed claims 46 and 51 are treatment claims, the method of assembling a tissue engineered construct of the currently examined claims comprise steps which are not required for or present in the method involving *ex vivo* gene therapy treatment claims. Thus, the operation, function and effects of these different methods are different and distinct from each other. The end results of each of these methods differ. Therefore, the inventions of these different, distinct groups are capable of supporting separate patents. Moreover, these methods have acquired a separate status in the art as shown by their different classification, class 514, subclass 44.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, new claims 46 and 51 in addition to claims 22-42 are withdrawn

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from consideration as being directed to non-elected inventions. See 37 CFR 1.142(b) and MPEP § 821.03.

***Response to Amendment***

The rejection of claims 1, 2, 4-8, 12, 13, 18 and 19 under 35 U.S.C. 102(b) as being anticipated by Sittinger et al. (US Patent No. 5,932,459) have been withdrawn in view of Applicant's amendment filed 21 July 2003.

Claims 1, 2, 4-21 and new claims 43-45 and 47 stand rejected under 35 U.S.C. 102(e) as being anticipated by Breitbart et al. (US Patent No. 6,077,987) for the reasons of record and those set forth below.

The rejection of claim 10 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been withdrawn in view of Applicant's amendment filed 21 July 2003.

***New Grounds of Rejection Necessitated by Applicant's Amendment***

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 48-50 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Breitbart, as previously cited, in view of Naughton et al. (US Patent No. 5,785,964).

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Breitbart et al. disclose a method for making a tissue construct comprising cells transformed with a growth factor that are seeded onto a biocompatible matrix comprising either synthetic or non-synthetic materials. See column 3 and column 8, lines 35-67. Breitbart teaches that a variety of cells may be transformed and grown on an extracellular matrix. See col. 8, lines 35-37 and column 2, line 60. Breitbart et al. disclose the use of several growth factors such as platelet-derived growth factor, vascular endothelial growth factor, insulin-like growth factor, epidermal growth factor and fibroblast growth factor, for example. See column 3, lines 55-60. Breitbart et al. fail to disclose that cells such as hepatocytes, Islet cells, and endothelial cells may be transfected and grown with an extracellular matrix such that a tissue engineered construct is formed.

Naughton et al. teach a three-dimensional cell culture system for the formation of a construct comprising a biocompatible extracellular matrix and cells such as bone marrow, liver and pancreas cells.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a tissue engineering construct comprising transformed hepatocytes (liver cells), endothelial cells (bone marrow cells) or Islet cells (pancreas cells) and a biocompatible extracellular matrix. As taught by Naughton et al. these cell types may be adhered and proliferated on three dimensional extracellular matrices because extracellular matrices provide a greater surface area for attachment and the adherence of cells. See column 7, line 60 to column 8, line 23. Moreover, Breitbart et al. disclose that a variety of cell types may be transfected and grown on three dimensional matrices as well. See col. 8, lines 35-37 and column 2, line 60. Breitbart et al. also teach growth factors that are effective for various cell types including

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hepatocytes, endothelial cells, and Islet cells such as VEGF, IGF-1 and endothelial derived growth supplement. See column 3, lines 50-60. Given the teachings of the art, the ordinary skilled artisan would have been motivated to grow transformed hepatocytes, endothelial cells or Islet cells in the presence of appropriate growth factors on extracellular matrices. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4-21 and new claims 43-45 and 47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description requirement is established by 35 U.S.C. 112, first paragraph which states that the: “*specification* shall contain a written description of the invention. . .[emphasis added].” A specification must convey to one of skill in the art that “as of the filing date sought, [the inventor] was in possession of the invention.” See *Vas Cath v. Mahurkar* 935 F.2d 1555, 1560 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Applicant may show that he is in “possession” of the invention claimed by describing the invention with all of its claimed

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limitations “by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention.” See *Lockwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

Applicant’s claims recite “a material that promotes cell adhesion.” The instant claims are drawn to a broad genus of compounds or compositions, which have the activity of promoting cell adhesion. These are genus claims that encompass a wide array of molecules. However, the specification does not disclose a representative number of species of “materials that promote cell adhesion.” The specification also fails to provide any teachings as to the structures or characteristics of this broad genus relate to their function such that one of skill in the art would reasonably conclude that Applicant was in possession of the invention claimed. Thus, the specification does not describe the complete structure of a representative number of species. Neither does the specification describe a representative number of species in terms of structure and relevant identifying characteristics. Absent of such teachings and guidance as to the structure-function relationship of this genus, the specification does not describe the claimed genus in such full, clear, concise and exact terms so as to indicate that Applicant had possession of them at the time of filing of the present application.

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 recites the limitations “derivatives thereof” and “combinations thereof.” The present claim is vague and indefinite as to its metes and bounds because it would be inherently

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unclear what derivatives or combinations of integrins, cell adhesion sequences, basement membrane components, agar and collagen are. Taken to the logical conclusion, derivatives of any of these compounds could even be a single carbon atom. Thus, one of skill in the art would not be apprised of the metes and bounds of the claim. "Combinations thereof" is also a phrase that leads to an unclear claim. This term does not clearly indicate if applicant is referring to combinations of agar and collagen only; all the "materials that promote cell adhesion," or what and to what degree any of these materials are combined. Moreover, Applicant's disclosure fails to provide adequate definition of these terms to define these terms to one of skill in the art.

### ***Response to Arguments***

Claims 1, 2, 4-21 and new claims 43-45 and 47-52 stand rejected under 35 U.S.C. 102(e) as being anticipated by Breitbart et al. (US Patent No. 6,077,987) for the reasons of record and those set forth below.

With regard to the present rejection Applicant argues: (1) that Breitbart et al. fail to disclose a matrix that has been coated with a material that promotes cell adhesion; (2) that Breitbart et al. fail to disclose that chondrocytes may be transfected with IGF-1.

At the outset Applicant should note that claims are given their broadest reasonable interpretation in light of the specification in light of the supporting disclosure. *In re Morris*, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997). Applicant argues that coating requires that the material that promotes cell adhesion should be "covered in a layer of a material that promotes cell adhesion." Breitbart et al. in fact disclose collagen, which is known to be



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involved in cell adhesion. Any matrix comprised of this material will necessarily be covered in a layer of collagen; thereby meeting the limitation of the claims.

Applicant additionally argues that Breitbart et al. fail to disclose chondrocytes transfected with IGF-1 only with TGF-beta or CGF. Applicant is directed to column 8, lines 35-37 and column 2, line 60 which teach a number of cells including chondrocytes that may be transfected with growth factors. Also, Applicant is directed to column 6, line 34 which teach in addition to TGF-beta and CGF, cells may be transformed with IGF-1. Thus, meeting these limitations of the claims as well.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.


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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Konstantina Katcheves whose telephone number is (703) 305-1999. The examiner can normally be reached on Monday through Friday 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-3388.

Konstantina Katcheves  
September 29, 2003



JAMES KETTER  
PRIMARY EXAMINER